

Clinical knots

HIV associated eosinophilic folliculitis—differential diagnosis and management

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Eosinophilic folliculitis (EF) is a chronic, intensely pruritic condition of unknown pathogenesis that causes marked morbidity in those HIV patients whom it affects. There is a wide differential diagnosis of itchy skin conditions in HIV which are amenable to different treatments. It is therefore essential to take a biopsy of each suspected case and examine multiple sections of the biopsy to confirm or refute a diagnosis of EF. Treatment of EF can be difficult but we hope that by suggesting a rational approach to this and considering possible therapeutic options more patients may be helped with this troublesome dermatosis.

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Introduction

Eosinophilic pustular folliculitis was originally described by Ofuji *et al.*¹ It was not until 1986 that it was first recognised to occur in the human immunodeficiency virus (HIV) infected population.² In this group it is now referred to as HIV associated eosinophilic folliculitis (EF) as it shows differences from the original Japanese description in its distribution, appearance of lesions, disease course, and symptoms. EF is not unique to HIV as it has rarely been described in association with haematological malignancies.³

Clinical picture

Patients affected by EF classically complain of a persistent pruritic rash. The intensity of the itch is akin to that of scabies and patients excoriate deeply. Clinically, one can see 2–3 mm erythematous papules or pustules, most frequently affecting the shoulders, trunk, upper arms, neck and forehead, where it can be disfiguring (fig 1). Less commonly, other areas of the body are affected but EF is only rarely generalised. Lesions are follicular and are often markedly excoriated, making it difficult to determine their nature. It is therefore important to look for fresh unexcoriated lesions. There are no associated systemic features but patients are often tired and irritable.

EF is quite common, occurring in HIV infected individuals with a CD4 count of less than $250 \times 10^6/l$ with an incidence, in one series, of 9%.⁴ Up to 50% of sufferers will have a peripheral eosinophilia, up to $4 \times 10^9/l$ in our series and their IgE is often also elevated.

Differential diagnosis

Clinically the differential diagnosis of EF is between the infective folliculitides or other dermatoses that may or may not be HIV related—for example, scabies, urticaria, drug rashes, and eczema. Clues in the history and the examination can help refine the diagnosis (table 1). Of note we feel that it is inappropriate to make a diagnosis of papular eruption of

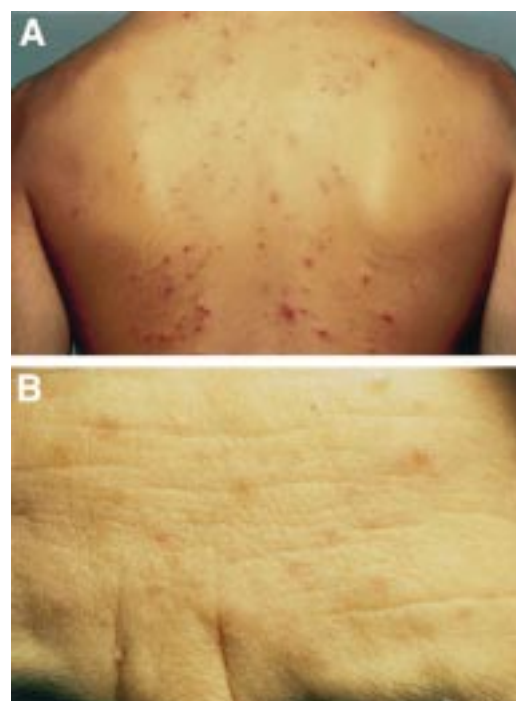


Figure 1 (A) Back of patient suffering from EF. Note the multiple excoriation marks. (B) Close up of a patient's forehead demonstrating the characteristic erythematous follicular papules of EF.

HIV as most cases will turn out to be EF if investigated appropriately.

Investigation of EF

Owing to the wide differential diagnosis of EF we always recommend that a skin biopsy is taken and sent for histology for routine haematoxylin and eosin stain as well as for special stains for fungi, bacteria, and viruses, as cutaneous infections can present with atypical clinical features. The biopsy should, if possible, be taken from an unexcoriated fresh lesion and serially sectioned. Sellotape strippings for demodex mites and scrapings for scabies should also be performed if there is any clinical suspicion of these.

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Table 1 Ways of obtaining diagnosis of eosinophilic folliculitis

Differential diagnosis	Clues in history and examination
Infestations: Scabies	Nighttime itching Partner itching Genital and web space lesions present No facial lesions
Papular urticaria (insect bite reactions)	Crops of linearly arranged papules Pets at home, hostel accommodation, or of no fixed abode ?Lice on seams of patient's clothes
Atopy: Urticaria Eczema	Individual weals lasting 6–12 hours ?Family or personal history of atopy Flexural rash
Iatrogenic: Drug rash	New drug within past 10–14 days Generalised rash
Other: Nodular prurigo Lichen planus/nitidis	Nodular rather than papular lesions lasting months/years Flat topped purple papules with Wickham's striae ?Any buccal or genital lesions

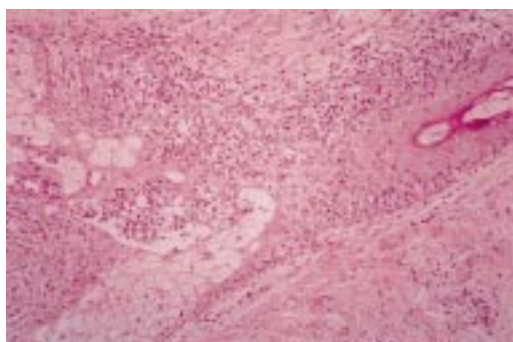


Figure 2 Medium power of haematoxylin and eosin stained section showing an infiltrate of eosinophils and lymphocytes centred on the follicle with marked sebaceous lysis.

Histology of EF

The histology of EF⁵ shows an inflammatory infiltrate, predominantly of eosinophils and lymphocytes which is folliculocentric with marked sebaceous lysis (fig 2). This is distinct from infective causes of folliculitis—for example, Gram positive cocci, demodex, and pityrosporum when micro-organisms are seen within the inflammatory infiltrate (macrophages and neutrophils). The affected follicle is frequently ruptured in a bacterial folliculitis. The histopathologist should be asked to take multiple serial sections of the EF biopsy as otherwise the affected follicle may be missed and the incorrect diagnosis made.

Pathogenesis of EF

The pathogenesis of EF is unknown but, owing to the folliculocentric nature of the inflammation, an opportunistic infection has been

proposed although no one organism has consistently been isolated in biopsy specimens. Fungi, yeasts, demodex, and bacteria have all at times been seen and implicated. Other theories are of a follicular hypersensitivity reaction or an autoimmune reaction to sebum (L A Fearfield, in preparation).

Treatment of EF

Treatment of EF is difficult and varied because the underlying pathogenic mechanism of EF still remains to be elucidated. Treatments tried have included topical steroids, topical acaricides—for example, permethrin, phototherapy (ultraviolet A and B light), itraconazole, isotretinoin, and metronidazole. All have had reported successes but the series reported have tended to be of small size and anecdotal rather than controlled or randomised. We discuss the different modalities below and our recommendations for treatment are shown in table 2.

TOPICAL STEROIDS

These can give partial temporary symptomatic relief but new lesions continue to crop up. For example, 0.1% betamethasone valerate (Betnovate, Glaxo), can be useful as a temporary measure when awaiting the results of the biopsy.

ANTIHISTAMINES

The anti-eosinophilic cetirizine (Zirtek, Schering-Plough) gives modest symptomatic relief especially if higher than usual dosages are used—for example, 20–40 mg daily in divided doses.

ULTRAVIOLET B PHOTOTHERAPY

Patients often report an improvement in symptoms after sunny holidays abroad and ultraviolet B is established as an effective treatment.⁶ Patients mostly respond to thrice weekly broad band ultraviolet B within 3–6 weeks. Relapse is frequent and weekly maintenance ultraviolet B may be needed. Ultraviolet B exerts an immunosuppressive effect on the skin and herpes simplex virus is reactivated in some. Earlier fears of accelerating progression of HIV disease have not been borne out.

ITRACONAZOLE

It has been suggested, by some authors, that fungi or yeasts—for example, *Pityrosporum ovale* may be involved in the pathogenesis of EF. This is certainly supported by the response of EF to oral itraconazole. In one study, by Berger *et al*, of 28 patients 74% showed initial complete or partial response to oral itraconazole. At 3 months five remained clear off treatment, two required topical steroids only, and 12 were controlled (n=8) or partly controlled with oral itraconazole.⁷ It is suggested that itraconazole is started at a dose of 200 mg daily. A response is normally seen within the first 2 weeks but if this has not occurred or the response is incomplete then the dose may be increased to 300 mg or 400 mg daily although the incidence of side effects is then increased. Maintenance therapy may be necessary. Fluconazole is not a substitute for itraconazole as patients changed to this drug relapsed.⁷

Table 2 Management of eosinophilic folliculitis

Short term management
(1) Biopsy, then while awaiting result: (2) Topical steroid—for example, 0.1% betamethasone valerate ointment (3) Antihistamine—for example, cetirizine 20–40 mg daily
Long term management
4 week trial of itraconazole 200 mg once daily or metronidazole 250 mg three times daily or referral to a dermatologist for ultraviolet B 2–3 times/week to clearance +/- maintenance or isotretinoin 20–40 mg daily for 4–6 weeks

METRONIDAZOLE

Metronidazole 250 mg three times daily for 4 weeks was reported to be effective in clearing EF in five out of five patients initially⁸ and following any subsequent relapse. This followed the finding of a Gram negative organism on one of the patient's biopsies.

ISOTRETINOIN

In an initial study in 1995⁹ all of the seven patients treated demonstrated complete response within 1–4 weeks of starting isotretinoin treatment at a dose of 40–80 mg/day (higher doses were given for those patients who were more severely affected). Any relapses responded to repeat courses of isotretinoin. (It must be remembered that isotretinoin is teratogenic and therefore should be used only with extreme caution in women of childbearing age.)

In our experience it is a very effective and well tolerated treatment using a lower dose of 20 mg daily for 6–8 weeks. The usual side effect of drying of the skin can be counteracted by the liberal use of moisturisers. The mechanism of action may be to reduce perifollicular cellular infiltration but the drug greatly curtails sebum production, which Fearfield has proposed as the putative autoantigen in EF.

PERMETHRIN

The commensal follicle mite, demodex, is a possible trigger antigen. A small series of patients have responded to topical 5% permethrin cream used daily on lesions and were able to control the disease eventually with one or two applications per week but upon cessation of treatment lesions recurred,¹⁰ but we have been unable repeat such success.

ANTIRETROVIRAL THERAPY

We have seen a marked decrease in the number of patients with EF in our clinics since the

introduction of highly active antiretroviral therapy (HAART), although there have not been any reports of this in the literature. This is probably because patients' CD4 counts usually rise above $250 \times 10^6/l$ on HAART.

OTHERS

Topical sodium cromoglycate, topical antibiotics, prednisolone, and dapsone have also been successfully used in some patients.

Contributors: SLS-D wrote the paper; LAF performed the research project and provided references and clinical and histopathological pictures; RCDS supervised the research project and the paper.

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